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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/028,245	12/18/2001	Nigel Dunn-Coleman	GC700	2138

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EXAMINER	
RAO, MANJUNATH N	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 10/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/028,245	DUNN-COLEMAN ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,4-17,19,20,22-24 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *23 and 24* is/are allowed.

6)☒ Claim(s) *2,4-17,19,20,22 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

CONTINUED EXAMINATION UNDER 37 CFR 1.114 AFTER FINAL REJECTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7-20-04 and 8-3-04 has been entered.

Claims 2, 4-17, 19-20, 22-24 and 26 are now currently pending in this application and are under consideration.

Applicant's amendments and arguments filed on 7-20-04, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. Specifically, Examiner has withdrawn the previous rejection of claim 1, 6 under 35 U.S.C. 112, 1st paragraph in view of claim cancellation. Examiner has also withdrawn the previously held rejection of claims 1, 6-7 as obvious over Bhikhabhai et al. in view of cancellation of claim 1 and persuasive arguments (N-terminal sequence and total amino acid profile of the proteins) provided by the applicants. However, it should be noted that applicants have neither cancelled nor amended claims 6 and 7.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete all the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. It is noted that applicant has deleted only " http://". However, the inclusion of "www" can still invoke the browser. Hence Examiner urges applicants to spell out "world wide web" and delete the "www".

Sequence Compliance

Applicant is required to comply with the sequence rules by inserting the sequence identification numbers of all sequences recited within the claims and/or specification. It is particularly noted that applicant has now included a new SEQ ID NO:5. However, the specification provides for only four sequences. Applicant is urged to cancel SEQ ID NO:5. See particularly 37 CFR 1.821(d).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 6-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 6 continues to depend from claim 1 which has been cancelled by the applicant, rendering the claim indefinite. Correction is required.

Claim 8 and claims 9, 11, which depend therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 8 recites the phrase "intermediate to high stringency". The metes and bounds of the above phrase is not clear to the Examiner in the context of the above claim. A perusal of the specification did not provide any definition for the above phrase or specific hybridization conditions with reference to the above phrase thus rendering the claim indefinite. Examiner suggests deletion of the above phrase and replacing with just "high stringency".

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 2 and claims 5, 10, 12-17, 19-20 which depend from claim 2 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 2 is drawn to an isolated nucleic acid molecule "encoding a polypeptide having 85% sequence identity to the amino acid sequence presented in SEQ ID NO:5". However, a perusal of the specification indicates that applicants have no support for "SEQ ID NO:5" which now constitutes a "new matter". Therefore claim 2 and claims 5, 10, 12-17, 19-20 which depend from claim 2 are rejected for introducing "new matter" into the claims.

In the remarks section of their response, applicants mention that they are aware of the requirement of new sequence listing. However, to this date, applicants have filed no such amended sequence listing pointing out appropriate support for the same in the specification.

Claims 2, 5, 8-17, 19-20, 22, 26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide isolated from *T.reesei*, with SEQ ID NO:1 or 4 encoding a polypeptide with SEQ ID NO:2 having endoglucanase, (EGVIII), activity and a method of making said endoglucanase, by transforming a host cell with an expression vector comprising the polynucleotide with SEQ ID NO:1 or 4 followed by cultivating the host cells and recovering the expressed endoglucanase, and being enabling for a recombinant host cell in which the polynucleotide with SEQ ID NO:1, 4 has been inactivated such that it does not express a functional endoglucanase, does not reasonably provide enablement for such a polynucleotide isolated from any source, or a polynucleotide encoding polypeptides with endoglucanase activity, and having 85%, 90%, or 95% sequence identity to SEQ ID NO:2 (or SEQ ID NO:5?) or such polynucleotides that hybridize under "intermediate to high stringency" conditions to a probe (of any length) designed to hybridize with the nucleotide sequence disclosed in figure 1, vectors and host cells comprising such polynucleotides, and a method of making said encoded endoglucanase, by transforming a host cell with an expression vector comprising the said polynucleotides followed by cultivating the host cells and recovering the expressed endoglucanase, or a recombinant host cell which does not express a functional endoglucanase, of any fungi. The specification does not enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 2, 5, 8-17, 19-20, 22, 26 are so broad as to encompass any polynucleotide from any source encoding an endoglucanase, vectors host cells and methods of expressing said endoglucanase and a recombinant host cell in which the polynucleotide encoding the endoglucanase is inactivated. Claims are also so broad because they encompass any variant or mutant polynucleotides encoding polypeptides that have 85%, 90%, or 95% sequence identity to SEQ ID NO:2 (or SEQ ID NO:5?). The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claims.

Claims 2 and 26 are drawn to any polynucleotide including mutants, variants and recombinants encoding any endoglucanase (even though applicants coin the term EGVIII) from any or all source. The "source" comprises a large group of plants, animals and microorganisms including several hundreds and thousands of members. They are also highly varied in their nutrition requirements and growth conditions. Applicants have provided support in their specification for isolation of a polynucleotide encoding an endoglucanase only from a single

fungal source. Applicants have not taught a universal method of isolation and characterization of polynucleotides encoding endoglucanases from any or all members of the "source". While methods to cultivate a good number of microorganisms are well known in the art, there is no universal single method for cultivating, testing and isolating endoglucanase from any or all species. As stated earlier, members of the group are diverse with varied nutritional and growth requirements. Therefore, it would be undue experimentation for those skilled in the art to test each and every species for polynucleotides encoding endoglucanase using the method provided by the applicants which applies to only a single fungal species, *Trichoderma*. Applicants have not shown that the method they have used for isolation of the polynucleotide from *Trichoderma* can be successfully used for each and every source that are known and unknown to man.

On similar lines, while applicants have provided SEQ ID NO:1 and 4 and host cells comprising such polynucleotides, and those skilled in the art would be enabled to inhibit such host cells from expressing endoglucanse encoded by SEQ ID NO:1 or 4 by going in and making changes to SEQ ID NO:1 or 4 (claim 22), they have not provided methods to do the same with host cells expressing any endoglucanase because applicants have not provided methods to isolate such polynucleotides in the first place. Therefore without such polynucleotides, those skilled in the art would be unable to make host cells containing such polynucleotides in the first place. Furthermore, applicants have also not taught a universal method that can be used to inactivate any fungal polynucleotide encoding endoglucanase in any host cell. Therefore claims drawn to host cells in which polynucleotides encoding endoglucanase are inactivated remain non-enabled.

With respect to claims directed to variant polynucleotides encoding polypeptides that have 85%, 90%, or 95% sequence identity to SEQ ID NO:2 (SEQ ID NO:5?), applicants have not taught those skilled in the art as to how to make and select the claimed polynucleotides, which leads to undue experimentation for those skilled in the art. Since the amino acid sequence of a protein encoded by a given polynucleotide, determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence to obtain the desired activity, requires a knowledge of and guidance with regard to which specific amino acids in the protein's sequence, if any, are tolerant to modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only a single endoglucanase, obtained from *T.reesei* and having an amino acid sequence SEQ ID NO:2 . Putting it in simpler terms, the specification is silent regarding the specific amino acids or specific regions in the amino acid sequence of SEQ ID NO:2 that can be modified (by insertion, deletion or substitution) without affecting the endoglucanase activity which could be used to construct variant polynucleotides. Therefore, it would require undue experimentation by a skilled artisan to identify such regions that can be changed and make and use all the claimed variant polynucleotides. The specification is limited to teaching the use of just SEQ ID NO:1 or 4 as polynucleotides encoding the polypeptide with SEQ ID NO:2. In view of the great breadth of the claim, amount of experimentation required to make the claimed polynucleotides, the lack of a universal method of isolating polynucleotides encoding an endoglucanase from any fungi and lack of guidance regarding where to make the changes in the polypeptide/nucleotide sequences,

working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495) to make a polynucleotide sequence, the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to make and use the full scope of the polynucleotides encompassed by this claim.

While recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass polynucleotides encoding endoglucanase from any or fungi, polynucleotide encompassing any or all modifications and fragments encoding a polypeptide with 85%, 90%, or 95% identity to the SEQ ID NO:2 or polynucleotides that hybridize under intermediate to high stringency conditions to a probe (of any length or function) designed to hybridize to the polynucleotide with SEQ ID NO:1, because the specification does not establish: (A) a single universal method to isolate polynucleotides encoding endoglucanse from any source ; (B) a single universal method to inactivate polynucleotides encoding endoglucanse from any source in any host cell; (C)regions in the polynucleotide structure which may be modified without effecting its activity of encoding a

functional endoglucanase; (D) the general tolerance of said polynucleotide sequence to modification and extent of such tolerance; (E) a rational and predictable scheme for modifying any nucleotide in any polynucleotide with an expectation of obtaining the desired biological function; and (F) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including polynucleotides from any fungi or polynucleotides with an enormous number of modifications of to the polynucleotide encoding the amino acid with SEQ ID NO:2 (SEQ ID NOS:1 or 4). The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polynucleotides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous Office action, applicants have traversed the above rejection. First of all Examiner notes that applicants submit that they have cancelled claim 1,(which they have actually done) and amended claim 2 to recite 90%, 95% or 98% sequence identity to SEQ ID NO:5? (a new matter issue) or 95% sequence identity to SEQ ID NO:2. However, it can be seen from the claims that applicants have not amended claim 2 to recite 90%, 95% or 98% sequence identity to SEQ ID NO:5? (a new matter issue). That said, it is not clear to the Examiner as to what applicants intend to do at this point.

Next, in response to Examiner's assertion regarding the unpredictability in the art applicants submit a reference (Mosimann et al.) and argue that the author indicates wherever the sequence identity between the target and the template is greater than 70%, comparative molecular modeling is high successful. While appreciating the conclusion in the reference, Examiner respectfully disagrees with such an argument, because the author never specifically discusses endoglucanase polypeptides.

Applicants also point out that Examiner asserts that "it is not routine in the art to screen for multiple modifications" and that applicants have provided assays for quickly measuring endoglucanase activity and that using any of the well known techniques such as MALDI-TOF, one can routinely sequence a protein and therefore what is well known in the art, needs not be taught in the specification. In view of such argument, Examiner has changed his previous argument (see above rejection). Furthermore, while it can be agreed that techniques are available to those skilled in the art, in order to make variants as claimed by the applicants, guidance is required. Such guidance is not provided by the applicants. As previously stated the specification does not establish: (A) a single universal method to isolate polynucleotides encoding endoglucanse from any source; (B) a single universal method to inactivate polynucleotides encoding endoglucanse from any source in any host cell; (C)regions in the polynucleotide structure which may be modified without effecting its activity of encoding a functional endoglucanase, EGVIII; (D) the general tolerance of said polynucleotide sequence to modification and extent of such tolerance; (E) a rational and predictable scheme for modifying any nucleotide in any polynucleotide with an expectation of obtaining the desired biological

function; and (F) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Therefore the above rejection is maintained.

Claims 22, 26 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This claim is directed to a genus of DNA molecules encoding endoglucanase from any or all sources, and a method of producing endoglucanase, using said DNA molecules in a *Aspergillus* host cell.

The specification does not contain any disclosure of the structure of all DNA sequences that are encompassed by the claims. The genus of DNAs that comprise these above DNA molecules is a large variable genus with the potentiality of having many different structures. Therefore, many structurally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

In response to the previous Office action, applicants have traversed the above rejection arguing they have cancelled claim 1 rendering the rejection moot for that claim and as to the other claims applicant notes that they are directed to a specific set of naturally occurring enzymes with endoglucanase activity. Next applicants also argue it is not necessary to teach that which is well known in the art etc. Applicants also note that it is not necessary under 35 U.S.C. 112 that every claimed embodiment be specifically exemplified and that a skilled artisan would be able to glean from the specification the metes and bounds of the invention. Applicants also note that the number of polypeptides encoded by the polynucleotides encompassed by the present claims is finite and well within the skill of the ordinary artisan. Examiner respectfully disagrees with all the above arguments and reiterates that they do not address the written description requirements. As discussed in the written description guidelines, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species which are adequately described are representative of the entire genus. **Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.** Satisfactory disclosure of a representative number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the

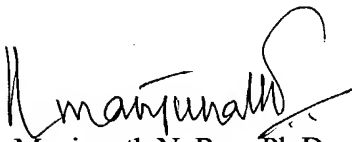
genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. In the instant case the claimed genera of Claims and 6 includes species which are widely variant in function. The genus Claims 22 and 26 are structurally diverse as it encompasses all polynucleotides encoding polypeptides with endoglucanase activity. As such, neither the description of the structure and function of SEQ ID NO:1 nor the disclosure solely functional features present in all members of the genus is sufficient to be representative of the attributes and features of the entire genus. Hence the above rejection is maintained.

Conclusion

None of the claims except 23-24 are allowable.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 571-272-0939. The Examiner can normally be reached on 7.00 a.m. to 3.30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned is 703-872-9306/9307 for regular communications and for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.



Manjunath N. Rao, Ph.D.
Primary Examiner
Art Unit 1652

October 14, 2004